

U.S. Application Ser. No. 10/532,258
Response to Restriction Requirement

Attorney Docket No. 662031(51588)

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Restriction Requirement

Restriction is required under 35 U.S.C. §121 and 372. The Examiner alleges that there are seven separate inventions, enumerated in seven groups set forth on pages 2-3 of the Office Action. The Examiner has required Applicants to elect one of the 7 groups for prosecution on the merits.

Applicants respectfully traverse the requirements for restriction and election, and submit that the requirements are improper. In particular, the Examiner has failed to apply correctly PCT Rule 13.2

Claims are unified if they share one or more special technical features that define a contribution that the invention makes over the prior art (Rule 13.2). The assessment of unity of invention, therefore, identifies the salient technical features of the claims and then determines whether that combination of features is disclosed in a given prior art document. The Examiner has neither identified the salient technical features of the claims, nor has the Examiner determined that the combination of features is taught or suggested in the prior art.

The methods set out in Group 1 are directed to methods of selecting a zinc finger polypeptide. The methods set out in Groups 2, 4, 5 and 7 are directed to methods of employing the zinc finger polypeptides or methods of preparing the zinc finger polypeptides, selected according to the method as set forth in Group 1. Groups 3 and 6 are directed to the zinc finger polypeptide and a library of zinc finger polypeptides, wherein the zinc finger polypeptides are selected according to the methods of claim 1. Accordingly, the claims should be unified under the PCT criteria as the claimed methods of selecting a zinc finger polypeptide are new and inventive over those disclosed in the prior art.

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Group 1 includes claims 1-39, and is drawn to a method of selecting a zinc finger polypeptide. Group 2 includes claim 40, 42, 45, 87, 89, and 92, and is drawn to a method of regulating the expression of a gene using a zinc finger polypeptide. Group 3 includes claim 41, 43, 44, 88, 90 and 91, and is drawn to a zinc finger polypeptide fused to one or more domains. Group 4 includes claims 46 and 93 and is drawn to a method of altering the structure of a gene using a zinc finger polypeptide. Group 5 includes claims 47 and 94, and is drawn to a method of cleaving a sequence of interest using a zinc finger polypeptide. Group 6 includes claims 95 and is drawn to a library of zinc finger polypeptides. Group 7 includes claims 48-86 and is drawn to a method of generating fusion proteins comprising zinc finger polypeptides and other functional domains.

Applying the requirements of PCT Rule 13.1, the claims of the present application are linked by the same or a corresponding special technical feature: a method of selecting a zinc finger polypeptide that binds to a sequence of interest comprising at least two subsites, wherein the method includes the step of: a) incubating position-sensitive primary libraries with target site constructs under conditions sufficient to form first binding complexes, wherein the primary libraries comprise zinc finger polypeptides having one variable finger and at least one anchor finger, and wherein the target site construct has one subsite with a sequence identical to a subsite of the sequence of interest, and one or more subsites with sequences to which the anchor finger(s) bind; b) isolating pools comprising nucleic acid sequences encoding polypeptides, wherein the polypeptides comprise the first binding complexes; c) **recombining the pools to produce a secondary library**; d) incubating the secondary library with the sequence of interest under conditions sufficient to form second binding complexes; and e) isolating nucleic acid sequences encoding zinc finger polypeptides, wherein said polypeptides comprise the second binding complexes.

These features represent several important concepts that underlie the method of selecting a zinc finger polypeptide of the present invention, and are novel and inventive and represent a contribution over the art, in particular, a method of selecting a zinc

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finger binding protein that includes the steps of 1) identifying pools of candidate zinc finger/subsite pairs and 2) **recombining the pools to produce a secondary library** comprising variants that harbor fingers which have been partially optimized for binding to a desired subsite. This recombination step is not simply amplification of a library.

A secondary library according to the invention can comprise a range of multi-finger protein composed of random combinations of the pools of fingers selected from the randomized fingers of the primary library. Thus, the secondary library can comprise multi-finger proteins that, unlike the primary library, can potentially vary at all finger positions of the multi-finger proteins. The secondary library of the invention can comprise fingers with a range of binding affinities and specificities for their target subsite.

The Examiner asserts at page 3 of the Office Action that Wolfe et al. (Structure 2008 Vol. 8: 739-750) "teach combinatorial libraries of zinc finger proteins derived from Zif268. The Wolfe reference also teaches selecting or screening for zinc finger proteins from a library of zinc finger proteins.

Applicants assert that the Wolfe et al. reference does not teach or suggest the claimed method of identifying a zinc finger polypeptide that includes the steps of 1) identifying pools of candidate zinc finger/subsite pairs and 2) **recombining the pools to produce a secondary library**, as described herein above, and in the instant specification, for example at paragraphs 0138-0140.

Accordingly, the requirements for restriction and election are improper and Applicants respectfully request that the requirements be withdrawn. Moreover, there would be no burden on the Examiner in searching and examining all the claims in a single application.

Nevertheless, in compliance with the directives in the Office Action and in order to expedite prosecution of the instant application, Applicants hereby provisionally elect,

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subject to the foregoing traverse, Group 1, encompassing claims 1-39, drawn to a method of selecting a zinc finger polypeptide.

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The Examiner has requested that Applicants elect a single ultimate species for each of the following:

- A. A single specific number of "zinc fingers" (for Groups 1-7);
- B. A single specific type of zinc finger polypeptide (for Groups 1-7); and
- C. A single specific "functional domain" fused to the zinc finger polypeptide (For Groups 3-5 and 8).

Applicants hereby elect three as the specific number of "zinc fingers" and the Cys2His2 zinc finger polypeptide as a single specific type of zinc finger polypeptide.

If the Examiner is disposed to making the restriction requirement final, Applicants respectfully request that the Examiner contact Applicants' attorney by telephone at (617) 239-0575 before issuing a first substantive Office Action.

CONCLUSION

Applicants respectfully submit that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at the telephone number shown below.

Dated: August 28, 2008

Respectfully submitted,

By Elizabeth N. Spar
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